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FORM PTO-1390 (Modified) (REV 5-93) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 058315/0129

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1 5):

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP96/03199	**July 19, 1996**	**July 19, 1996**

TITLE OF INVENTION
VIRAL INTERLEUKIN 6

APPLICANT(S) FOR DO/EO/US
Bernhard FLECKENSTEIN, Jens-Christian ALBRECHT, Frank NEIPEL, Alvin FRIEDMAN-KIEN, and Yao-Qi HUANG

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☐ A translation of the International Application into English (35 U.S.C. 371 (c)(2)).

7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.

8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.

14. ☐ A substitute specification.

15. ☐ A change of power of attorney and/or address letter.

16. ☐ Other items or information:

U.S. APPLICATION NO (If known, see 37 C.F.R. 1.50	INTERNATIONAL APPLICATION NO. PCT/EP96/03199	ATTORNEY'S DOCKET NUMBER 058315/0129

17. ☒ The following fees are submitted:

		CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5): Search Report has been prepared by the EPO or JPO . . . . **$840.00** International preliminary examination fee paid to USPTO (37 CFR 1.482) . . . . **$670.00** No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2) . . . . . **$760.00** Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO . . . . **$970.00** International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) **$96.00**			
ENTER APPROPRIATE BASIC FEE AMOUNT =		$ **840.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e))		$ **0.00**	

Claims	Number Filed	Number Extra	Rate		
Total Claims	28 -20 =	8	X $18.00	$ **144.00**	
Independent Claims	12 -3 =	9	X $78.00	$ **702.00**	
Multiple dependent claim(s) (if applicable)			+ $260.00	$ **0.00**	

TOTAL OF ABOVE CALCULATIONS =	$ **1,686.00**	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).	$ **0.00**	
SUBTOTAL =	$ **1,686.00**	
Processing fee of **$130.00** for furnishing English translation later the ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f). +	$ **0.00**	
TOTAL NATIONAL FEE =	$ **1,686.00**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$ **0.00**	
TOTAL FEES ENCLOSED =	$ **1,686.00**	
	Amount to be: refunded	$
	charged	$

a. ☒ A check in the amount of $1,686.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 19-0741 in the amount of $ to the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 19-0741. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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Patricia D. Granados
SIGNATURE

Patricia D. Granados
NAME

33,683
REGISTRATION NUMBER

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Atty. Dkt. No. 58315/129**
Bernhard FLECKENSTEIN et al.	:	
Serial No.: Unassigned	:	
Filed: January 19, 1999	:	
For: VIRAL INTERLEUKIN-6		

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Prior to examination, please amend the above-identified application as follows:

IN THE CLAIMS:

Please cancel claims 21-27 without prejudice or disclaimer.

Please amend claims 1-20 as follows:

Claim 1, line 2: Delete "HHV-8" and insert --human herpes virus type 8 ("HHV-8")--.

Claim 2, line 2: Delete "displayed in" and insert --of--.

Claim 3, line 1: Delete "displayed in" and insert --of--.

Claim 4, line 1: Delete "IL-6" and insert --interleukin-6 ("IL-6")--.

Claim 5, line 1: After "which", insert --consists--; delete "comprises" and insert --of--.

Claim 6, line 1: Delete "or 5".

Claim 7, line 1: Delete "or of the polypeptide as"
line 2: Delete "claimed in claim 2,".

Claim 8, line 1: Delete "Fragments" and insert --A fragment--; delete "or the polypeptide as claimed in".

line 2: Delete "claim 2 or 3,"; delete "they" and insert --it is--.

9. (Amended) An isolated nucleic acid molecule coding for v-IL-6 [as claimed in claim 1], which is obtainable by recombinant expression of the DNA of human herpes virus type-8 (HHV-8).

10. (Amended) An isolated nucleic acid molecule coding for [the] a polypeptide [as claimed in claim 2], which is obtainable by recombinant expression of the DNA of HHV-8 and which comprises the amino acid sequence of Fig. 2.

Claim 11, line 1: Delete "displayed in" and insert --of--.

Claim 12, line 1: After "acid", insert --molecule--.

line 2: Delete "one or more of the claims 9 to" and insert --claim--.

Claim 13, line 1: Delete "directed against" and insert --which bind--; delete "," and insert --.--.

line 2: Delete the line.

Claim 14, line 1: After "comprising", insert --a container and--.

line 2: Delete "16" and insert --13--.

15. (Amended) Testkit for the detection of antibodies against v-IL-6, comprising [v-IL-6 as claimed in claim 1 and/or the] a polypeptide that binds said antibody [as claimed in claim 2 or 3 or both, claims 2 and 3, and/or mutants and variants of v-IL-6 as claimed in claim 7, and/or fragments of v-IL-6 as claimed in claims 4-6 or 8].

Claim 16, line 1: Delete "acic" and insert --acid molecule--.

line 2: Delete "one or more of claims 9 to 12" and insert --claim 11--.

17. (Amended) A [medicament] pharmaceutical composition comprising as an active ingredient [the] an IL-6-inhibiting an effective amount of an antibody as claimed in claim 13 and a pharmaceutically acceptable carrier.

18. (Amended) A [medicament] pharmaceutical composition comprising as an active ingredient [v-IL-6 as claimed in claim 1 and/or] the polypeptide as claimed in claim 2 [or 3, and/or mutants and variants of v-IL-6 as claimed in claim 7, and/or fragments of v-IL-6 as claimed in claim 4-6 or 8] and a pharmaceutically acceptable carrier.

19. A [medicament] pharmaceutical composition comprising as an active ingredient the nucleic acid as claimed in [one or more of claims 9 to 12] claim 11 and a pharmaceutically acceptable carrier.

Claim 20, line 1: Delete "as an additional active ingredient".
line 2: Delete ", or the polypeptide as claimed in claims 2 or 3, or mutants" and insert --.--.
line 3: Delete the line.
line 4: Delete the line.

Please add new claims 28-35 as follows:

--28. A fragment of a polypeptide that is obtainable by recombinant expression of the DNA of HHV-8 and which comprises the amino acid sequence of Fig. 2.

29. A monoclonal or polyclonal antibody which binds a polypeptide that is obtainable by recombinant expression of the DNA of HHV-8 and which comprises the amino acid sequence of Fig. 2, or a fragment thereof.

30. The testkit of claim 15, wherein said polypeptide is v-IL-6 or a fragment thereof.

31. An *in vitro* assay for the detection of v-IL-6, comprising contacting a sample suspected of containing v-IL-6 with an antibody that binds v-IL-6 and detecting said antibodies that bind said v-IL-6 in said sample.

32. The assay of claim 31, wherein said detecting of antibodies that bind said v-IL-6 indicates the presence of an HHV-8 in said sample.

33. The assay of claim 31, wherein said detecting of antibodies that bind said v-IL-6 indicates the presence of an HHV-8 in said sample.

34. A method of culturing cells, comprising adding to a cell culture comprising said cells a cell growth-stimulating amount of v-IL-6.

35. The method of claim 34, wherein said cells are selected from the group consisting of β-lymphocytes, hybridomas, hemopoetic and endothelial cells.--

REMARKS

The foregoing amendments eliminate multiple dependency and otherwise conform the claims to U.S. practice. No new matter is added.

Examination on the merits is respectfully requested.

Respectfully submitted,

January 19, 1999
Date

Patricia D. Granados
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Viral Interleukin-6

The present invention relates to viral interleukin-6 (v-IL-6), which can be obtained by recombinant expression of the DNA of human herpesvirus type 8 (HHV-8), and which may be used in diagnosis and treatment of human diseases such as kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma.

Kaposi's sarcoma (KS), a multifocal proliferative lesion of uncertain pathogenesis, is highly prevalent among homosexual AIDS patients. Studies with biopsy materials and cultured cells have indicated an important role of growth factors and cellular cytokines, such as basic fibroblast growth factor, interleukin-1β, platelet derived growth factor, interleukin-6 (IL-6), and oncostatin M for the proliferation of spindle cells in KS [1,2]. Several groups found indication for the expression of interleukin-6 (IL-6) receptors in AIDS-KS cells [3] and derived spindle cell lines [4]. As epidemiological evidence had suggested that an infectious agent other than HIV may also be involved in KS pathogenesis, it stirred considerable interest when Chang and colleagues [5] found DNA sequences of a novel herpesvirus in AIDS-KS tissues. Meanwhile, DNA of this virus was consistently found in all epidemiological forms of KS. The new virus, termed human herpesvirus 8 (HHV-8), shows marked sequence homology to *herpesvirus (h.) saimiri*, the prototype of γ_2-herpesviruses; thus HHV-8 appears to be the first human

member of γ_2-herpesviruses (genus rhadinovirus). Cloning HHV-8 DNA from KS tissues and sequencing indicates a genome organization that is generally collinear to *h. saimiri* [6].

In the course of these studies we surprisingly found, adjacent to a dihydrofolate reductase gene, an open reading frame (ORF) with the coding capacity for a 204 amino acid polypeptide with marked homology to mammalian IL-6 (P-value for homology searches with NCBI-BLAST: $P \leq 10\text{-}18$; percent identity/similarity to human IL-6: 24.74%/ 46.91%; to murine: 24.23%/ 47.94%; to porcine: 25.97%/ 52.91%; to bovine: 24.60%/ 49.73%; all alignments were calculated with the GCG software "GAP").

The viral gene product (v-IL-6) has conserved all 4 cysteine residues that are known to be involved in IL-6 disulfide bridging, and it shows a characteristic signal peptide of 19 to 22 amino acids (fig. 1). The area involved in binding of human IL-6 to its receptor has been mapped to the middle of the protein by two groups[7, 8, 9]. Ehlers et al. showed that amino acids 105 to 123 of the human IL-6, as shown in fig. 1 (GFNEEtCLVKIitGLLEFE), are involved in receptor binding. Most remarkably, this region is highly conserved in v-IL-6 (GFNEtsCLkKLadGFFEFE). Identity and similarity of v-IL-6 to the receptor binding region of human IL-6 are 58% and 74%, respectively (fig. 1). This is almost identical with the degree of conservation that can be observed in this receptor binding area of human IL-6 to murine IL-6. As both human IL-6 and murine IL-6 are able to bind to the receptor of the other species (murine IL-6 and human IL-6, respectively), it is likely that v-IL-6 is also able to bind to the human and the murine IL-6 receptor.

Rhadinoviruses frequently acquire genes from their host cell [10]. This HHV-8 ORF however, is the first known example of a viral IL-6 structural homologue. Up to now all cell-homologous genes of rhadinoviruses that have been tested were functional; non-functional genes would most likely have been lost in viral evolution. Thus, the conservation of essential IL-6 features makes it highly suggestive that v-IL-6 is

functional in normal HHV-8 replication or persistence. Since models of paracrine growth stimulation of spindle cells by cytokines, including IL-6 and the related oncostatin M, have been proposed for KS pathogenesis, the finding of the v-IL-6 gene in HHV-8 lends support to the hypothesis that HHV-8 is causally related to this multifocal proliferation.

The present invention therefore relates to:

a) Viral interleukin-6 (v-IL-6), which can be obtained by recombinant expression of the DNA of HHV-8.

b) A polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2.

c) A fragment of v-IL-6, having the capability of binding to an IL-6 receptor and comprising the amino acid sequence GFNEtsCLkKLadGFFEFE.

d) A fragment as defined in b1, which essentially comprises the amino acid sequence GFNEtsCLkKLadGFFEFE.

e) A fragment as defined in c or d, which binds to a human IL-6 receptor.

f) A polypeptide having the amino acid sequence displayed in fig. 2.

g) Mutants and variants of v-IL-6 or of the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2, which mutants and variants are obtained by conventional amino acid substitutions or deletions, with the proviso that these mutants and variants are functionally equivalent to v-IL-6.

h) Fragments of v-IL-6, or of the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2, characterized in that they are able to competively inhibit the biological activity of IL-6 in a suitable assay system.

i) An isolated nucleic acid coding for v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2. A preferred embodiment is the nucleic acid having the nucleotide sequence of fig.2. Furthermore, an isolated nucleic acid, hybridizing to the abovementioned nucleic acids under stringent conditions and encoding functionally active v-IL-6 shall be comprised.

k) Monoclonal or polyclonal antibodies directed against v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2.

l) Testkit for the detection of v-IL-6 in a sample, comprising one or more of the above monoclonal or polyclonal antibodies.

m) Testkit for the detection of antibodies against v-IL-6 comprising v-IL-6 and/or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2, and/or mutants and variants of v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2 and/or fragments of v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2.

n) Testkit for the detection of v-IL-6 DNA or RNA, comprising a nucleic acid which codes for v-IL-6, or which hybridizes to the aforementioned nucleic acid and encodes functionally active v-IL-6.

o) A medicament comprising as an active ingredient a monoclonal antibody or polyclonal antibodies directed against v-IL-6, or a polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2, or mutants, variants or fragments of v-IL-6 or the aforementioned polypeptide. In another embodiment, the medicament may comprise as an active ingredient a nucleic acid encoding v-IL-6.

p) A cell culture growth medium, comprising as an active ingredient v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2 , or mutants, variants or fragments of v-IL-6 or the aforementioned polypeptide.

q) A process of manufacturing v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2, or mutants and variants, or fragments of v-IL-6 or the aforementioned polypeptide.

r) A process of manufacturing a medicament, wherein the active ingredient is combined with suitable excipients and/or other auxilliary compounds according to common knowledge of those skilled in the art. .

s) A process of manufacturing a medicament comprising as an active ingredient monoclonal or polyclonal antibodies directed against v-IL-6, or a polypeptide comprising v-IL-6, or mutants, variants or fragments of v-IL-6, or a nucleic acid encoding v-IL-6 for the treatment of kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma.

t) A process of diagnosing an HHV-8 infection comprising the in vitro detection of v-IL-6 antigen, v-IL-6 DNA, v-IL-6 RNA or antibodies against v-IL-6.

u) A process of diagnosing the HHV-8 associated disorders kaposi sarcoma, Castleman's disease or body cavity based lymphomas (BCBL) through the diagnosis of an HHV-8 infection as described above.

v) A process of growing cells in culture, characterized in that v-IL-6 or the polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2, or mutants and variants, or fragments of v-IL-6 or the aforementioned polypeptide, or mixtures of these compounds are contained in the growth medium. In a preferred process these cells are B-lymphocytes, hybridomas, hemopoetic cells or endothelial cells.

The sequence shown in fig.2 was generated by first subcloning shotgun fragments of lambda clone G16 into commercially available plasmid pBS KS- (Stratagene, San Diego, califormia). Resulting plasmids were purified using a commercially available kit (Qiagen, Hilden, Germany) and sequenced on an automated sequencing system (A377, Applied Biosystems GmbH, Weiterstadt, Germany) using the recommendations of the manufacturer. The sequence was determined on both strands, using standard primers for shotgun clones, and gene specific primers for further analysis. In addition to showing the coding sequence of the interleukin-6 homologue of human herpesvirus 8, the deduced amino acid sequence, in one and three letter code, is shown in the sequence listing below.

The present invention is further described in the claims.

Bibliography:

1. Miles, S. A. et al.: *Science,* 255, 1432-1434 (1992).
2. Stürzl, M. et al.: Oncogene 10, 2007-2016 (1995).
3. Miles, S. A. et al.: Proc. Natl. Acad. Sci. U. S. A. 8
4. Masood, R. et al.: AIDS Res. Hum. Retroviruses 1
5. Chang, Y. et al.: Science. 266, 1865-1869 (1994)
6. Moore, P. S. et al.: J. Virol. 70, 549-558 (1996).
7. Hammacher, A. et al.: Protein Sci. 3, 2280-2293
8. Ehlers, M. et al.: J. Immunol. 153, 1744-1753 (1994).
9. Ehlers, M. et al.: Ann. N.Y. Acad. Sci. 762, 400-402 (1995).
10. Albrecht, J. C. et al.: J. Virol. 66, 5047-5058 (1992).

Legends:

Figure 1:

Alignment of the sequences of the predicted protein precursor of the HHV-8 IL-6 gene with human and mouse IL-6. Amino acids identical in all three proteins are indicated by an asterisk, cysteine residues involved in disulfide bridging are marked with an arrowhead. Upper case letters symbolize amino acids conserved according to the criteria defined by M. Dayhoff.

Figure 2:

Nucleic acid sequence encoding v-IL-6 and corresponding amino acid sequence.

Claims:

1. Viral interleukin-6 (v-IL-6), which can be obtained by recombinant expression of the DNA of HHV-8.

2. A polypeptide, which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in fig. 2.

3. A polypeptide having the amino acid sequence displayed in fig. 2.

4. A fragment of v-IL-6, having the capability of binding to an IL-6 receptor and comprising the amino acid sequence GFNEtsCLkKLadGFFEFE.

5. A fragment as claimed in claim 4, which essentially comprises the amino acid sequence GFNEtsCLkKLadGFFEFE.

6. A fragment as claimed in claim 4 or 5, which binds to a human IL-6 receptor.

7. Mutants and variants of v-IL-6 as claimed in claim 1, or of the polypeptide as claimed in claim 2, which mutants and variants are obtained by conventional amino acid substitutions or deletions, with the proviso that these mutants and variants are functionally equivalent to v-IL-6.

8. Fragments of the v-IL-6 as claimed in claim 1, or the polypeptide as claimed in claim 2 or 3, characterized in that they able to competively inhibit the biological activity of IL-6 in a suitable assay system.

9. An isolated nucleic acid coding for v-IL-6 as claimed in claim 1.

10. An isolated nucleic acid coding for the polypeptide as claimed in claim 2.

11. An isolated nucleic acid having the nucleotide sequence displayed in fig. 2.

12. An isolated nucleic acid, hybridizing under stringent conditions to the nucleic acid as claimed in one or more of the claims 9 to 11, encoding functional v-IL-6.

13. Monoclonal or polyclonal antibodies directed against v-IL-6 as claimed in claim 1, or the polypeptide as claimed in claim 2 and/or 3.

14. Testkit for the detection of v-IL-6 in a sample, comprising an antibody as claimed in claim 16.

15. Testkit for the detection of antibodies against v-IL-6, comprising v-IL-6 as claimed in claim 1 and/or the polypeptide as claimed in claim 2 or 3 or both, claims 2 and 3, and/or mutants and variants of v-IL-6 as claimed in claim 7, and/or fragments of v-IL-6 as claimed in claim 4-6 or 8.

16. Testkit for the detection of v-IL-6 DNA or RNA, comprising a nucleic acic as claimed in one or more of the claims 9 to 12.

17. A medicament comprising as an active ingredient the antibody as claimed in claim 13.

18. A medicament comprising as an active ingredient v-IL-6 as claimed in claim 1 and/or the polypeptide as claimed in claim 2 or 3, and/or mutants and variants of v-IL-6 as claimed in claim 7, and/or fragments of v-IL-6 as claimed in claim 4-6 or 8.

19. A medicament comprising as an active ingredient the nucleic acid as claimed in in one or more of claims 9 to 12.

20. A cell culture growth medium, comprising as an additional active ingredient v-IL-6 as claimed in claim 1, or the polypeptide as claimed in claim 2 or 3, or mutants and variants as claimed in claim 7, or fragments as claimed in claim 8, or mixtures of these substances.

21. A process of manufacturing v-IL-6 as claimed in claim 1, or the polypeptide as claimed in claim 2 or 3, or mutants and variants as claimed in claim 7, or fragments as claimed in claim 4-6 or 8.

22. A process of manufacturing a medicament, wherein v-IL-6 as claimed in claim 1, or the polypeptide as claimed in claim 2 or 3, or mutants and variants as claimed in claim 7, or fragments as claimed in claim 8 are combined with suitable excipients and/or other auxilliary compounds.

23. A process of manufacturing a medicament comprising as an active ingredient monoclonal or polyclonal antibodies directed against v-IL-6, or a polypeptide comprising v-IL-6, or mutants, variants or fragments of v-IL-6, or a nucleic acid encoding v-IL-6 for the treatment of kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma.

24 An process of diagnosing an HHV-8 infection comprising the in vitro detection of v-IL-6 antigen, v-IL-6 DNA, v-IL-6 RNA or antibodies against v-IL-6.

25. A process of diagnosing the HHV-8 associated disorders kaposi sarcoma, Castleman's disease or body cavity based lymphomas (BCBL) through the diagnosis of an HHV-8 infection as claimed in claim 24.

26. A process of growing cells in culture, characterized in that v-IL-6 as claimed in claim 1, or the polypeptide as claimed in claim 2 or 3, or mutants and variants as claimed in claim 7, or fragments as claimed in claim 4-6 or 8, or mixtures of these compounds are contained in the growth medium.

27. The process as claimed in claim 26, wherein the cells are B-lymphocytes, hybridomas, hemopoetic cells or endothelial cells.

Fig. 1:

```
                1                                                      56
Il6 human       MnsFStsaFgPVAFsLGLLLVlpaAFPapvppgeDskDvaaPhRQpLTsSErIDkq
Il6 mouse       MkFLSaRdFhPVAF.LGLMLVttTAFPtsqvrRGDFtEdttPnRpVyTtSQ.VGgl
Il6 hhv8        McWFklWsL....LlVGsLLVsgT........RGkLpDapefeKDLLi......qr
 Consensus      *               *  **

               57                                                      112
Il6 human       IrYILdgIsaLRKEtCNKsnMCeSskEALAENNLnLPkMaEkDGCFQsGFNEEtCL
Il6 mouse       IthVLWeIvEMRKELCNgnSdCmnndDALAENNLKLPeIqrnDGCYQtGYNQEiCL
Il6 hhv8        LnWMLWvIdEcfRDLCyRtGICkGilEpaAifhLKLPaInDtDhCgliGFNEtsCL
 Consensus          *  *       *     *       *   * **     * *   * *   **
                               ^     ^                      ^         ^
               113                                                     168
Il6 human       VKIitGLLEFEVYLEYLqNrF.EsSeEqARaVQMsTKvLIQFLQkkaKNLdaIttP
Il6 mouse       LKIssGLLEYhsYLEYMkNnLkDnkkDkARVLQrdTeTLIHIFnQEVKDLhKIvlP
Il6 hhv8        kKLadGFFEFEVlFkFLtteF.GkSvinvdVMELlTKTLgwdIQEELnkLtKthys
 Consensus       *   *  *                          *  *          *

               169                                                     223
Il6 human       dPttNASLLtKLQAQnQWLqdmTtHLILRSFkEFLqssLRaLRQM.........
Il6 mouse       tPisNAlLtDKLESQKEWLRtkTiQFILKSLEEFLkvtLRstRQt.........
Il6 hhv8        pPkfDrGLLGRLQGlKyWVRhfasfYVLsaMEkFagqaVRvLdsIpdvtpdvhdk
 Consensus       *     *   *     *         *     *     *
```

Fig. 2:

SEQUENCE LISTING

1.	Sequence characteristics:		
	1.1.	Length:	612 base pairs
	1.2.	Type:	Nucleic Acid
	1.3.	Strandedness:	Double stranded
	1.4.	Topology:	Linear
2.	Molecule type:		Genomic DNA
3.	Description:		Human herpesvirus 8 interleukin-6 gene
4.	Hypothetical:		No
5.	Anti-sense:		No
6.	Original source:		Kaposi Sarkoma from HIV positive donor
7.	Organism:		Human herpesvirus 8

```
  1  ATG TGC TGG TTC AAG TTG TGG TCT CTC TTG CTG GTC GGT TCA CTG
  1   M   C   W   F   K   L   W   S   L   L   L   V   G   S   L
  1  Met Cys Trp Phe Lys Leu Trp Ser Leu Leu Leu Val Gly Ser Leu

 46  CTG GTA TCT GGA ACG CGG GGC AAG TTG CCG GAC GCC CCC GAG TTT
 16   L   V   S   G   T   R   G   K   L   P   D   A   P   E   F
 16  Leu Val Ser Gly Thr Arg Gly Lys Leu Pro Asp Ala Pro Glu Phe

 91  GAA AAG GAT CTT CTC ATT CAG AGA CTC AAT TGG ATG CTA TGG GTG
 31   E   K   D   L   L   I   Q   R   L   N   W   M   L   W   V
 31  Glu Lys Asp Leu Leu Ile Gln Arg Leu Asn Trp Met Leu Trp Val

136  ATC GAT GAA TGC TTC CGC GAC CTC TGT TAC CGT ACC GGC ATC TGC
 46   I   D   E   C   F   R   D   L   C   Y   R   T   G   I   C
 46  Ile Asp Glu Cys Phe Arg Asp Leu Cys Tyr Arg Thr Gly Ile Cys

181  AAG GGT ATT CTA GAG CCC GCT GCT ATT TTT CAT CTG AAA CTA CCA
 61   K   G   I   L   E   P   A   A   I   F   H   L   K   L   P
 61  Lys Gly Ile Leu Glu Pro Ala Ala Ile Phe His Leu Lys Leu Pro

226  GCC ATC AAC GAT ACT GAT CAC TGC GGG TTA ATA GGA TTT AAT GAG
 76   A   I   N   D   T   D   H   C   G   L   I   G   F   N   E
 76  Ala Ile Asn Asp Thr Asp His Cys Gly Leu Ile Gly Phe Asn Glu

271  ACT AGC TGC CTT AAA AAG CTC GCC GAT GGC TTT TTT GAA TTC GAG
 91   T   S   C   L   K   K   L   A   D   G   F   F   E   F   E
 91  Thr Ser Cys Leu Lys Lys Leu Ala Asp Gly Phe Phe Glu Phe Glu

316  GTG TTG TTT AAG TTT TTA ACG ACG GAG TTT GGA AAA TCA GTG ATA
106   V   L   F   K   F   L   T   T   E   F   G   K   S   V   I
106  Val Leu Phe Lys Phe Leu Thr Thr Glu Phe Gly Lys Ser Val Ile

361  AAC GTG GAC GTC ATG GAG CTT CTG ACG AAG ACC TTA GGA TGG GAC
121   N   V   D   V   M   E   L   L   T   K   T   L   G   W   D
121  Asn Val Asp Val Met Glu Leu Leu Thr Lys Thr Leu Gly Trp Asp

406  ATA CAG GAA GAG CTC AAT AAG CTG ACT AAG ACG CAC TAC AGT CCA
136   I   Q   E   E   L   N   K   L   T   K   T   H   Y   S   P
136  Ile Gln Glu Glu Leu Asn Lys Leu Thr Lys Thr His Tyr Ser Pro

451  CCC AAA TTT GAC CGC GGT CTA TTA GGG AGG CTT CAG GGA CTT AAG
151   P   K   F   D   R   G   L   L   G   R   L   Q   G   L   K
151  Pro Lys Phe Asp Arg Gly Leu Leu Gly Arg Leu Gln Gly Leu Lys

496  TAT TGG GTG AGA CAC TTT GCT TCG TTT TAT GTT CTG AGT GCA ATG
166   Y   W   V   R   H   F   A   S   F   Y   V   L   S   A   M
166  Tyr Trp Val Arg His Phe Ala Ser Phe Tyr Val Leu Ser Ala Met
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541  GAA AAG TTT GCA GGT CAA GCG GTG CGT GTT TTG GAC TCT ATC CCA
181   E   K   F   A   G   Q   A   V   R   V   L   D   S   I   P
181  Glu Lys Phe Ala Gly Gln Ala Val Arg Val Leu Asp Ser Ile Pro

586  GAC GTG ACT CCT GAC GTC CAC GAT AAG
196   D   V   T   P   D   V   H   D   K
196  Asp Val Thr Pro Asp Val His Asp Lys
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Docket No. 058315/0129

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

VIRAL INTERLEUKIN 6

the specification of which is attached hereto unless the following box is checked:

☒ was filed on ***July 19, 1996*** as United States Application Number or PCT International Application Number ***PCT/EP96/03199*** and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATION(S)

NUMBER	COUNTRY	DAY/MONTH/YEAR FILED	PRIORITY CLAIMED

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

APPLICATION NO.	FILING DATE

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

I hereby appoint as my attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Stephen A. Bent, Reg. No. 29,768; David A. Blumenthal, Reg. No. 26,257; William T. Ellis, Reg. No. 26,874; John J. Feldhaus, Reg. No. 28,822; Patricia D. Granados, Reg. No. 33,683; John P. Isacson, Reg. No. 33,715; Donald D. Jeffery, Reg. No. 19,980; Eugene M. Lee, Reg. No. 32,039; Richard Linn, Reg. No. 25,144; Peter G. Mack, Reg. No. 26,001; Brian J. McNamara, Reg. No. 32,789; Sybil Meloy, Reg. No. 22,749; George E. Quillin, Reg. No. 32,792; Colin G. Sandercock, Reg. No. 31,298; Bernhard D. Saxe, Reg. No. 28,665; Charles F. Schill, Reg. No. 27,590; Richard L. Schwaab, Reg. No. 25,479; Arthur Schwartz, Reg. No. 22,115; Harold C. Wegner, Reg. No. 25,258.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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